REMARKS/ARGUMENTS

Reconsideration of this application is requested. Claims 1-18, 20-42, 45 and 46 are in the case. Claims 1-18, 20-40, 45 and 46 are withdrawn from consideration.

Claims 41 and 42 are pending and under examination. By this Amendment claim 41 has been amended. Support for the amendment can be found in the subject application at US Publication No. 2001/0016576A1, paragraph 0157.

I. DOUBLE PATENTING

Claims 41 and 42 stand provisionally rejected on obviousness-type double patenting grounds as allegedly unpatentable over claims 1, 5 and 31 of co-pending application Serial No. 09/930,494. That rejection is respectfully traversed.

Claims 1, 5 and 31 of the co-pending application are similar to the claims having the same numbers in the present application, except for the dosage ranges. In the restriction requirement mailed March 28, 2003 in the present application, it was held that claims 41 and 42 are patentably distinct over claims 1, 5 and 31. Based on this, it is believed that the subject matter of claims 41 and 42 of the present application is not rendered obvious by the subject matter of claims 1, 5 and 31 of the '494 application and that, therefore, claims 41 and 42 are patentably distinct from claims 1, 5 and 31 of the '494 application. In light of this, it is believed that the outstanding obviousness-type double patenting rejection should be withdrawn. Such action is respectfully requested.

II. THE 35 U.S.C. §112, FIRST PARAGRAPH, REJECTION

Claims 41 and 42 stand rejected under 35 U.S.C. §112, first paragraph, on the ground that the specification, while enabling for the treatment of taxol induced neuropathy, allegedly does not reasonably provide enablement for the treatment of side effects induced by all other cancer chemotherapy agents. This rejection is respectfully traversed.

It is believed that the specification is fully enabling with respect to the invention as claimed in this application. However, in order to expedite prosecution, and without conceding to the merit of the Examiner's position, claim 41 has been amended to insert "related to mitochondrial dysfunction" after "chemotherapy agents". Basis appears at page 31 of the specification, second complete paragraph. No new matter is entered.

The undersigned has been advised that the toxic effects of most cyotoxic cancer chemotherapy agents are due to mitochondrial damage (topoisomerase inhibitors, for example topotecan, irinotecan and etoposide, are exceptions). It has already been demonstrated that a number of chemotherapy agents have deleterious effects on mitochondria, either by inhibiting respiratory chain activity or by damaging mitochondrial DNA. The damage to mitochondria may be significant enough to contribute to toxic side effects of chemotherapy. Among chemotherapy agents already demonstrated to have deleterious effects on mitochondria are:

- Platinum drugs, e.g. cisplatin (Am J Physiol. 1990 May; 258 (5 Pt 2): F1181-7. Mitochondrial injury: an early event in cisplatin toxicity to renal proximal tubules. Brady H.R., Kone B.C., Stromski M.E., Zeidel M.L., Giebisch G., Gullans S.R.,

Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts 02115).

- Alkylating agents, e.g. cyclophosphamide (Mutat Res. 2002 Apr 25;501(1-2):29-36. Dietary modulation of mitochondrial DNA deletions and copy number after chemotherapy in rats. Branda R.F., Brooks E.M., Chen Z., Naud S.J., Nicklas J.A., Department of Medicine, University of Vermont, 32 N. Prospect Street, Burlington, VT 05405, USA).

- Anthracyclines, e.g. doxorubicin (Toxicol Appl Pharmacol. 1994 Dec;12 9 (2):214-22, Disruption of mitochondrial calcium homeostasis following chronic doxorubicin administration. Solem L.E., Henry T.R., Wallace K.B., Department of Pharmacology, University of Minnesota, Duluth 55812).

- Bleomycin (Mutat Res. 2002 Mar 20;500(1-2):1-8. Molecular analysis of mitochondrial DNA mutations from bleomycin-treated rats. Khaidakov M., Manjanatha M.G., Aidoo A., Division of Genetic and Reproductive Toxicology, National Center for Toxicological Research, Jefferson Laboratories of the FDA, Jefferson, AR 72079, USA).

- Mitomycin C (Oncol Res. 1997;9(6-7):333-7. A new cellular target for mitomycin C: a case for mitochondrial DNA. Pritsos CA, Briggs LA, Gustafson DL. Department of Nutrition, University of Nevada, Reno 89557, USA).

- Reviews: e.g., Pharmacol Ther. 1992;54(2):217-30. Mitochondrial DNA damage by anticancer agents. Singh G., Sharkey S.M., Moorehead R., OCF, Hamilton Regional Cancer Center, Ontario, Canada; Mutat Res. 2003 Apr 9;525(1-2):19-27. Changes in the human mitochondrial genome after treatment of malignant disease, Wardell T.M., Ferguson E., Chinnery P.F., Borthwick G.M., Taylor R.W., Jackson G.,

Craft A., Lightowlers R.N., Howell N., Turnbull D.M., Department of Neurology, The Medical School, University of Newcastle upon Tyne, Newcastle upon Tyne NE2 4HH, UK. (full-length copies of Wardell et al. and Singh et al. and abstracts of the other publications are attached).

Based on the above, it is believed that the invention as now claimed is fully enabled by the present specification. Reconsideration and withdrawal of the outstanding lack of enablement rejection are accordingly respectfully requested.

Favorable action on this application is awaited.

Respectfully submitted,

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Attachments: Wardell et al., Singh et al., Abstracts of Brady et al., Branda et al., Solem et al., Khaidakov et al. and Pritsos et al.; PTO 1449